EXHIBIT 1, Tab 6b

5.2.2 HYDROTHERAPY

Hydrotherapy is one of the oldest forms of treatment for patients with arthritis. Despite this, formal evidence showing benefit is sparse. Limited evidence suggests that hydrotherapy can effect and maintain an improvement in self-efficacy in addition to some clinical and psychological gain.[172, 173] A recent systematic review of balneotherapy[174] (i.e. hydrotherapy or spa therapy) noted that no conclusion could be provided from the reviewed studies due to poor methodology. Further well-conducted trials are needed to assess the efficacy of this mode of treatment.

5.2.3 OTHER PHYSICAL THERAPIES

Evidence for other therapies such as the application of ice or heat,[175] TENS or laser therapy[176–179] is conflicting or is insufficient to support their routine use. There is limited evidence showing symptomatic benefit from ultrasound.[180]

5.3 SPLINTING

Splinting can be undertaken by occupational therapists, physiotherapists, or orthotists. Good evidence to support the use of resting hand splinting is sparse although two studies did report a significant reduction in pain when splints were applied.[181,182] Wrist working splints have been shown to decrease pain on activity[183,184] but do not improve function, grip strength or dexterity.[185,186] There is no good evidence to support the use of splints to correct ulnar deviation or any other deformity.

Evidence level 1+

Resting and working splints can be used to provide pain relief.

5.4 PODIATRY

The importance of appropriate footwear provision for comfort, mobility and stability is well recognised in clinical practice but there is little evidence-based research to support such observations in patients with early RA.

There is some evidence regarding the efficacy of foot orthoses in terms of both comfort level and stride speed and length.[187–189]

The guideline development group could find no research regarding other podiatry interventions such as reduction of callosities and padding of the feet in those with early RA.

☑ Podiatry referral should be offered to all patients.

5.5 DIETETICS

Nutritional advice plays an important part in the management of a patient with RA. Enquiries about diet are amongst those most commonly received from patients.

5.5.1 WEIGHT MANAGEMENT

Weight reduction in obese individuals is important particularly when weight bearing joints are involved. Management should be as recommended in the SIGN guideline on obesity.[190]

Cachexia may occur in those with severe active RA. The aetiology is likely to be multifactorial. Several studies have shown that patients with low body mass index (BMI) do less well and have poorer functional status.[191,192] Whilst it is not clear whether dietary intervention improves outcome, for general health reasons, an adequate BMI should be maintained. Some patients will require diet supplements in addition to dietary advice.

5.5.2 DIET AS THERAPY

Relatively few studies have been carried out to assess the effect of diet therapy on disease activity in RA.[193] Fasting has been shown to be of benefit in some patients.[194] Weight loss often occurs and this may not be beneficial in all patients. Practical difficulties have also been encountered in implementing and maintaining strict dietary changes. The evidence regarding food exclusion is often anecdotal and is inconclusive. Exclusion/elimination diets can be difficult to follow and if adhered to over a long period of time, may lead to the development of nutritional deficiencies.

5.5.3 DIET SUPPLEMENTS

A meta-analysis of clinical trials of fish oil supplementation in RA concluded that there was a significant reduction in the number of tender joints and in duration of morning stiffness after three months of therapy. However, no effect was seen on indices of disease activity or progression of RA.[195] There are practical limitations to this approach, including the large quantities of fish oil required. The latter is expensive, difficult to take and not available on prescription.

The effect of other oils such as evening primrose oil[196] and blackcurrant seed oil[197] on disease activity in RA remains uncertain.

Annex 1

DETAILS OF SYSTEMATIC REVIEW UNDERTAKEN FOR THE GUIDELINE

The evidence base for this guideline was synthesised in accordance with SIGN methodology. A systematic review of the literature was carried out using an explicit search strategy devised by the SIGN Information Officer in collaboration with members of the guideline development group.

Searches were restricted to systematic reviews, meta-analyses, randomised controlled trials, and longitudinal studies. Inclusion criteria were patients with rheumatoid arthritis within five years of diagnosis, aged over 16. Exclusion criteria were studies based outside Western Europe, Scandinavia, North America, Australia or New Zealand; surgery; psychological treatments; social care or social support of patients.

Searches were carried out on the Cochrane Library, Embase, Medline, and Pascal from 1985 onwards. A subsearch on alternative or traditional therapies also looked at the Allied & Alternative Medicine and Mantis databases. All search strategies were evaluated by an independent information specialist.

The main searches were supplemented by material identified by individual members of the development group. All selected papers were evaluated using standard methodological checklists before conclusions were considered as evidence.

The question of late harm caused particular difficulties in searching. The section of the strategy on this topic focused on the long-term toxicity or toleration of DMARDs. It is recognised that this limited approach does not fully cover the literature on this subject, but given the restricted time available to complete the development process it was decided to accept this limitation.

Annex 2

AMERICAN RHEUMATISM ASSOCIATION 1987 REVISED CRITERIA FOR THE CLASSIFICATION OF RHEUMATOID ARTHRITIS[16]

Diagnosis of rheumatoid arthritis requires four of seven of the following criteria. In criteria one to four the joint signs or symptoms must be continuous for at least six weeks.

Signs & Symptoms	
1. Morning stiffness	Duration > 1hr lasting > 6 weeks
2. Arthritis of 3 or more joint areas*	Soft tissue swelling or effusion lasting > 6 weeks
3. Arthritis of hand joints	Wrist, metacarpophalangeal joints or proximal interphalangeal joints lasting > 6weeks
4. Symmetric arthritis*	At least one area, lasting > 6 weeks
5. Rheumatoid nodules	As observed by a physician
6. Serum rheumatoid factor	As assessed by a method positive in less than 5% of control subjects
7. Radiographic changes	As seen on anteroposterior films of wrists and hands

* *Possible areas: proximal interphalangeal joints, metacarpophalangeal joints, wrist, elbow, knee, ankle, metatarsophalangeal joints (observed by a physician).*

At least four criteria must be fulfilled.

Annex 3

CRITERIA FOR COMPLETE REMISSION IN RA

Complete remission is achieved with five of the following six:

1. morning stiffness < 15 minutes
2. no fatigue
3. no joint pain (history)
4. no joint tenderness or pain on motion
5. no soft tissue swelling in joint/tendon sheaths
6. Westergren ESR < 30mm/hr (F) < 20mm/hr (M)

Exclusion: extra-articular disease

Annex 4

HEALTH ASSESSMENT QUESTIONNAIRE[17]

Patient Label Date

We are interested in learning how your illness affects your ability to function in daily life. Please feel free to add any comments at the end of this form.

PLEASE TICK ONE RESPONSE WHICH BEST DESCRIBES YOUR USUAL ABILITIES OVER THE PAST WEEK:

	Without ANY difficulty	With SOME difficulty	With MUCH difficulty	Unable to do
	Score = 0	*Score = 1*	*Score = 2*	*Score= 3*
1. **DRESSING AND GROOMING** - ***Are you able to***				
Dress yourself, including tying shoelaces and doing buttons?				
Shampoo your hair?				
2. **RISING** - ***Are you able to***				
Stand up from an armless straight chair?				
Get in and out of bed?				
3. **EATING** - ***Are you able to***				
Cut your meat?				
Lift a full cup or glass to your mouth?				
Open a new carton of milk (or soap powder)?				
4. **WALKING** - ***Are you able to***				
Walk outdoors on flat ground?				
Climb up five steps?				

PLEASE TICK AIDS OR DEVICES THAT YOU USUALLY USE FOR ANY OF THESE ACTIVITIES:

Walking stick	Crutches
Devices for dressing e.g. buttonhook, zipper pull, long handled shoe horn	Special or built-up chair Wheelchair
Walking frame	Other (please specify)
Built-up or special utensils	

PLEASE TICK ANY CATEGORIES FOR WHICH YOU USUALLY NEED HELP FROM ANOTHER PERSON:

Dressing and grooming	Rising	Eating	Walking

HEALTH ASSESSMENT QUESTIONNAIRE *continued*

	Without ANY difficulty *Score = 0*	With SOME difficulty *Score = 1*	With MUCH difficulty *Score = 2*	Unable to do *Score= 3*
5. HYGIENE - *Are you able to*				
Wash and dry your entire body?				
Take a bath?				
Get on and off the toilet?				
6. REACH - *Are you able to*				
Reach and get down a 5lb object (e.g. a bag of potatoes) from above your head?				
Bend down to pick up clothing from the floor?				
7. GRIP - *Are you able to*				
Open car doors?				
Open jars which have been previously opened?				
Turn taps on and off?				
8. ACTIVITIES - *Are you able to*				
Run errands and shop?				
Get in and out of a car?				
Do chores such as vacuuming, housework or light gardening?				

PLEASE TICK AIDS OR DEVICES THAT YOU USUALLY USE FOR ANY OF THESE ACTIVITIES:

Raised toilet seat	Jar opener (for jars previously opened)	Long handled appliances for reach
Bath seat	Bath rail	Other (please specify)

PLEASE TICK ANY CATEGORIES FOR WHICH YOU USUALLY NEED HELP FROM ANOTHER PERSON:

Hygiene	Reach	Gripping and opening things	Errands and housework

SCORING OF HAQ

Add the maximum score for each of the 8 sections and divide by 8 to give a score between 0–3.

If aid/device or help is needed the score for that activity automatically = 2 *(unless 3 has already been ticked.)*

Normal function = 0

Most affected function = 3

Annex 5

EVALUATION OF DMARD EFFECT

1. ACR IMPROVEMENT CRITERIA[198]

- tender joint count*
- swollen joint count*
- at least three of:
  - global disease activity – investigator
  - global disease activity – patient**
  - patient assessment of pain
  - physical disability score, e.g. HAQ
  - acute phase reactant

ACR 20, ACR 50 and ACR 70 indicate 20%, 50% and 70% improvement in the above

* *extent of synovitis is measured by doing a count of number of tender joints and number which are both swollen and tender.*

** *patient opinion of disease activity measured on a 10 cm visual analogue scale. Anchor points at either end of the scale are 'not active at all' and 'extremely active'.*

2. EULAR RESPONSE CRITERIA[199]

Disease activity score (DAS) is derived using a nomogram which incorporates the following four measures:

- Ritchie articular index[200]
- swollen joint count
- ESR (Westergren)
- general health score

DAS > 2.8 is usual level of activity for enrolment in DMARD studies

Interpretation of change in disease activity score from baseline evaluation of response:

> 1.2 good

> 0.6 moderate ≤ 1.2

≤ 0.6 non-responder

3. RADIOLOGICAL ASSESSMENT

Sharp method[201] (scores erosions and joint space narrowing)

Larsen method[202] (utilises standardised films that illustrate progressive destructive disease)

Annex 6

Awareness of and vigilance for drug interactions is important, but concern about drug interactions should not prevent the prescription of drugs that are needed to reduce joint damage in early RA. Much more morbidity will accrue from leaving RA untreated than will occur as a result of these interactions.

DRUG INTERACTIONS WITH NSAIDs

Drug	Effect of NSAID on drug	Principal mechanism*
Antihypertensives (ACE Inhibitors, Angiotensin II receptor antagonists)	Therapeutic effect decreased Hyperkalaemia and renal impairment increased	Sodium retention Interference with intrarenal prostaglandins
Warfarin	Therapeutic effect increased	Displaced protein binding Inhibition of drug metabolism
Sulphonylureas	Therapeutic effect increased	Displaced protein binding
Cyclosporin	Risk of nephrotoxicity increased	
Methotrexate	Therapeutic effect increased	Reduced renal clearance
Digoxin	Therapeutic effect increased	Reduced renal clearance
Lithium	Therapeutic effect increased	Reduced renal clearance
Phenytoin	Therapeutic effect increased	Displaced protein binding

Risk of GI haemorrhage is increased in patients on warfarin or corticosteroids. Further interactions are listed in the British National Formulary, Appendix 1[58]

** the mechanisms underlying drug interactions are complex*

DRUG INTERACTIONS WITH DMARDs

Drug	Interacts with
Azathioprine	Allopurinol Co-trimoxazole, trimethoprim, rifampicin Possibly warfarin
Hydroxychloroquine	Amiodarone Antiepileptics Digoxin
Cyclosporin	Multiple drugs, grapefruit juice
D-penicillamine	Antacids, zinc, iron (including proprietary indigestion tablets or mixtures) *N.B. should not be taken together*
Sulphasalazine	Digoxin
Methotrexate	Aspirin/NSAIDs Co-trimoxazole, trimethoprim, phenytoin All antifolate drugs Cyclosporin
Leflunomide	Phenytoin Warfarin Tolbutamide Other hepatotoxic/haemotoxic drugs
Minocycline	Antacids, zinc, iron Cyclosporin

Further interactions are listed in the British National Formulary, Appendix 1[58]

Annex 7

EXTENT OF RESPONSE TO SINGLE AGENTS IN RECENT DMARD STUDIES

Drug	Dose	no. in study	median disease duration	median duration of study	proportion achieving response	
					ACR 20†	ACR 50†
Sulphasalazine[130]	2-3 g/day	68	1 year	1 year	59%	[34%]*
Sulphasalazine[85]	2 g/day	133	7 years	0.5 year	44%	30%
Methotrexate[130]	7.5-15 mg/day	69	1.5 years	1 year	59%	[38%]*
Methotrexate[96]	7.5-15 mg/day	182	6 years	1 year	35%	23%
Methotrexate[139]	7.5-20 mg/day	217	1 year	1 year	65%	42%
Leflunomide[85]	20 mg/day	133	8 years	0.5 year	48%	33%
Leflunomide[96]	20 mg/day	182	7 years	1 year	41%	34%
Etanercept[139]	10 mg twice weekly (subcutaneous)	208	1 year	1 year	64%	32%
Etanercept[139]	25 mg twice weekly (subcutaneous)	207	1 year	1 year	72%	48%

*figures in [ ] reflect Dougados report of EULAR "good" responders

† see Annex 5

Annex 8

RECOMMENDATIONS FOR FURTHER RESEARCH

The following are suggested as potential areas for further research:

GENERAL

1. The definition of early RA.
2. Clarification of the important factors for diagnosis and prognosis.
3. Inception cohort studies to investigate the combination of prognostic factors that will predict disease severity in individual patients and allow patients suitable for early aggressive therapy to be identified.
4. Evaluation of new imaging techniques to assess early joint damage.
5. Audit of referral time from symptom onset to rheumatology clinic appointment: resource implications of delay before specialist review.

PHARMACOLOGICAL MANAGEMENT

NSAIDs

1. Further evaluation of highly selective Cox2 agents:
   - will they reduce the incidence of ulcer complications in routine clinical practice?
   - will it be necessary for GI protective agents to be co-prescribed in patients at high risk of ulcer complications?
   - what effect will they have on NSAID- associated renal and cardiovascular events?
2. NSAIDs which block nitric oxide synthetase.

DMARDs

1. The optimum treatment strategy for achieving remission in early RA using existing/new DMARDs. This should include:
   - the most appropriate action if a patient fails to achieve an adequate response to methotrexate or sulphasalazine
   - long term, adequately powered studies of the combination of methotrexate and sulphasalazine in early disease
   - prospective study of other combination options
   - assessment of long term safety issues.

CORTICOSTEROIDS

1. Long term, adequately powered studies to investigate whether continuous low-dose prednisolone and step-down prednisolone regimens will reduce joint damage/disability in the long term.
2. Assessment of cumulative toxicity.

TNF BLOCKADE AND NOVEL THERAPIES

1. The role of anti-TNF therapy in the treatment of patients with early RA:
   - as 'bridge therapy' to induce remission while waiting for DMARDs to take effect
   - in combination with DMARD therapy when there has been insufficient beneficial effect
   - as monotherapy in RA
   - the optimal dosage and method of administration of anti-TNF therapy and the issue of immunogenicity

- efficacy of anti-TNF agents in preventing joint damage and maintaining function over the longer term
- long term data on whether anti-TNF therapy will increase susceptibility to infection or tumours
- pharmacoeconomic analyses of anti-TNF therapy including indirect costs associated with RA (e.g. disability and unemployment).

2. Evaluation of future possibilities for biological therapy in RA, such as:
   - IL-1 receptor blockade with recombinant human IL-1 receptor antagonist
   - blockade of IL-6 receptors
   - anti-inflammatory cytokines such as IL-10 and IL-4
   - targeting T-cells e.g. anti-CD4 antibodies.
3. Evaluation of matrix metalloproteinase inhibitors in early RA.

THE ROLE OF THE MULTIDISCIPLINARY TEAM

1. Evaluating early intervention by the multidisciplinary team versus medical care alone and the impact on functional ability.
2. Evaluation of rheumatology nurse specialist role.
3. Physiotherapy
   - compliance with exercise and its relationship to longer term outcome
   - the effect of exercise training programmes on muscle strength and function
   - inpatient versus outpatient physiotherapy in the management of early RA.
4. Occupational therapy
   - efficacy of joint protection techniques.
5. Splinting
   - short and longer term evaluation of resting and working splints.
6. Podiatry
   - effect of foot orthoses on foot deformity and pain.
7. Dietetics
   - RCTs of dietary supplements such as antioxidants
   - further research on the possible drug-sparing effect of fish oils.
8. Pharmacy
   - the role of the pharmacist in patient education about drug therapy
   - the pharmacist's role in monitoring for drug interaction and side effects.

PATIENT INVOLVEMENT

1. The emotional impact of being diagnosed with RA and the value of psychological input.
2. Assessment of patient attitudes to early aggressive treatment.
3. Strategies to try to maintain patient employment: vocational assessment and retraining if necessary.
4. RCTs of educational interventions including patient led self-management courses in early RA (evaluating their impact on disability and emotional distress).
5. RCTs of psychological therapy such as cognitive behavioural therapy in early RA (evaluating their impact on disability and emotional distress).

OTHER ASPECTS

1. RCTs of complementary therapies in early RA evaluating benefit and harm.
2. Homeopathy in early RA.

Annex 9

KEY MESSAGES FOR PATIENTS

These key messages are not intended for direct dissemination to patients, but are provided for possible use by clinicians in discussing treatment options with patients who have RA. They may be incorporated into local patient information materials, an example of which is shown in Annex 10.

- In RA joints become inflamed making them painful, swollen and stiff.
- The cause of RA is unknown.
- There is no single test to diagnose RA.
- RA cannot be cured at present, but in many cases it can be controlled.
- The progression of RA is different in each person.
- RA can be treated; reducing pain, stiffness, swelling and damage to joints.
- The sooner RA is treated the better, the earlier treatment is started the less damage takes place in the joints, meaning less restriction on carrying out normal activities.
- Treatment with DMARDs should begin as soon as possible after diagnosis.
- DMARDs take several weeks to start working and should be continued indefinitely.
- The treatment of RA requires input from a range of health professionals.

Annex 10

EXAMPLE PATIENT INFORMATION LEAFLET

WHAT IS RHEUMATOID ARTHRITIS (RA)?

RA is a disease that makes your joints become painful, swollen and stiff. This is caused by inflammation taking place in the joints. Inflammation is normally caused by our body's immune system when we are injured or have an infection. We do not know what causes the immune system to cause inflammation in the joints.

HOW IS RA DIAGNOSED?

There is no single test for diagnosing RA. The diagnosis is made from the information you give the doctor as well as the information gained from examining you and the results of blood tests and x-rays.

CAN RA BE CURED?

RA cannot be cured at present, but for many patients it can be controlled.

HOW WILL RA AFFECT ME IN THE FUTURE?

At present it is not possible to predict for an individual person how their RA will affect them in the future. Some people have very mild RA which causes few problems. Others have some pain and stiffness in their joints and occasional flare-ups when their joints become more painful and swollen. This can lead to damage to the joints. Some people will have to modify their activities in some way. A small number of people develop significant problems.

CAN RA BE TREATED?

Yes.

Treatment for RA can:

- help with the pain, stiffness and swelling in joints
- reduce damage to joints
- help people stay able to do all the things they want to.

HOW CAN RA BE TREATED?

Treating RA is a partnership between you, your GP and your rheumatologist. Treatment does not just involve taking tablets. A team of health professionals is also important. These include: nurse specialist, physiotherapist, occupational therapist, pharmacist, dietitian, podiatrist (chiropodist) and social worker.

You can help by knowing as much as you can about RA and its treatment. If you know about your tests, drugs and the need to watch for side effects, your outlook will be better.

WHEN SHOULD I START TREATMENT FOR RA?

The sooner the better.

The earlier treatment is started the less damage takes place in the joints and the more likely that you will be able to continue your usual activities.

WHAT MEDICATION SHOULD I HAVE?

- **Painkillers** such as paracetamol, cocodamol and coproxamol may help with pain. It is important that you do not take more than the maximum recommended dose. Painkillers other than paracetamol may cause constipation.
- **Nonsteroidal anti-inflammatory drugs (NSAIDs)** such as ibuprofen, diclofenac, naproxen, indomethacin, nabumetone, etodolac, meloxicam, rofecoxib and celecoxib, help with the pain, swelling and stiffness in your joints, but do not stop damage occurring to your joints. There are many different NSAIDs and not all NSAIDs suit everyone. You may have to try several different drugs before you find one that helps you. The main side effect of NSAIDs is indigestion. Sometimes inflammation or ulceration of the stomach or intestine can occur. This may very rarely cause bleeding. If you experience indigestion or have previously had a stomach ulcer you should discuss this with your doctor. Sometimes additional treatment to protect the gastrointestinal tract is needed.
- **Disease modifying anti-rheumatic drugs (DMARDs)** include sulphasalazine, methotrexate, gold, penicillamine, hydroxychloroquine, azathioprine, cyclosporin and leflunomide. You should start on a DMARD as soon as possible after being diagnosed with RA. DMARDs are not painkillers, but over time they should help with the pain and stiffness in your joints and make you feel better. DMARDs are very important because they slow down damage to your joints and reduce disability. DMARDs take some weeks to start working. It is important to continue taking them, even if they do not seem to be working at first. You will be fully informed about the potential risks and benefits of DMARDs. You will be given written information about any DMARD that your doctor has suggested you start. Most DMARDs require regular blood tests and sometimes urine tests in order to look out for side effects. You should be given a card or monitoring sheet on which the results of your blood tests can be recorded.
- **Steroid injections** into joints can help with the pain and swelling in that joint. Rest after injection may result in additional benefit. Sometimes when you have many inflamed joints, steroid will be given as an injection into your muscle.
- **Steroid tablets**, such as prednisolone, are sometimes necessary, but they have potential side effects. They help with symptoms and may prevent joint damage in the short term, but most people who are on steroid tablets for a long time suffer from side effects. These include thinning of bones (osteoporosis), thinning of skin and putting on weight.

HOW LONG SHOULD I CONTINUE ON TREATMENT?

Usually you should stay on treatment with a DMARD for as long as the drug continues to work, provided that you do not develop side effects which are serious or troubling. If this happens then an alternative DMARD will be recommended by your rheumatologist.
Most patients need to keep taking a DMARD in order to stop their arthritis from flaring up and to slow down damage occurring to the joints. Hopefully, if your joint pain improves on the DMARD then you will be able to take fewer painkillers and perhaps stop your NSAID.

SHOULD I EXERCISE OR NOT?

Exercise is important. It can reduce joint pain and stiffness and keep your muscles strong. This will improve your level of fitness and make you feel better. All patients with RA should see a **physiotherapist** for advice about suitable exercises which may be carried out on dry land or in water (hydrotherapy).

SHOULD I CONTINUE TO WORK?

It is important not to make decisions about work too soon. Modern therapy should allow control of your disease and continuation of employment even if hours and activities require modification.

WHAT OTHER TREATMENTS SHOULD I HAVE?

- **Occupational therapists** can advise you about different ways of carrying out many everyday activities. This helps to protect your joints. In addition you can be given simple aids to help with certain tasks.
- Wrist splints can help with pain.
- Footwear is important. Shoes that are comfortable and support your feet are helpful. You can be referred to a **podiatrist** (chiropodist) and/or orthotist to be supplied with cushioned insoles or better fitting shoes.
- It is helpful if you can be your ideal bodyweight. This is based on your height and your doctor or nurse specialist can advise you about this. A **dietitian** can give you advice about losing weight if you are overweight or putting weight on if you are too thin.

IS THERE A DIET THAT WILL HELP RA?

At present there is no evidence from scientific studies to support changing to any particular diet.

DO ANY HERBAL OR COMPLEMENTARY MEDICINES HELP RA?

Supplements of fish oil may help the symptoms of RA, but do not stop joint damage. Large quantities of fish oil are required. Other complementary medicines have not been shown to be of benefit in RA. Many complementary medicines have not been tested in good quality scientific studies. Complementary medicines may have side effects.

Annex 11

USEFUL ORGANISATIONS/SUPPORT GROUPS

ARTHRITIS RELATED ADDRESSES AND WEBSITES

Arthritis Canada — www.arthritis.ca

Arthritis Care — www.arthritiscare.org.uk
Phoenix House, 7 South Avenue, Clydebank
Business Park, Clydebank, G81 2LG
Tel: 0141 952 5433
Fax: 0141 952 5433

American College of Rheumatology — www.rheumatology.org

Arthritis Foundation of Ireland — www.arthritis-foundation.com
1 Clanwilliam Square, Grand Canal Quay, Dublin 2, Ireland
Tel: (+353) 01 6618188
Fax: (+353) 01 6618261

Arthritis Foundation (USA) — www.arthritis.org

Arthritis Research Campaign (ARC) — www.arc.org.uk
Copeman House, St Mary's Court, St Mary's Gate,
Chesterfield, Derbyshire S41 7TD
Tel: 01246 558033
Fax: 01246 558007

British Health Professionals in Rheumatology — www.rheumatology.org.uk/BHPR
c/o BSR, 41 Eagle St, London WC1R 4AR
Tel: 0171 242 3313
Fax: 0171 242 3277

British Society of Rheumatology — www.rheumatology.org.uk
41 Eagle Street, London WC1R 4AR
Tel: 020 7 242 3313
Fax: 020 7 242 3277
(includes the British Society for Rheumatology, British Institute of Musculoskeletal Medicine, British Orthopaedic Association, Society for Back Pain Research, the Arthritis and Rheumatism Council for Research)

European League Against Rheumatism (EULAR) — www.eular.org
EULAR Secretariat, Witikonerstrasse 15, CH-8032
Zürich, Switzerland
Tel: +41 1 383 96 90
Fax: +41 1 383 98 10

The British League against Rheumatism (BLAR)
c/o The British Society for Rheumatology (see above)

International League of Associations for Rheumatology (ILAR) — www.ilar.org

University of Birmingham, Dept of Rheumatology — www.rheuma.bham.ac.uk

OTHER USEFUL ADDRESSES AND WEBSITES

Disabled Living Foundation 380-384 Harrow Rd, London W9 2HU	www.dlf.org.uk
Health information distributed by GPs	www.healthinfocus.co.uk
Health Education Board for Scotland Woodburn House, Canaan Lane, Edinburgh EH10 4SG *Tel: 0131 536 5500* *Fax: 0131 536 5501*	www.hebs.scot.nhs.uk
Help for Help Trust (UK) Highcroft, Romsey Road, Winchester, Hampshire SO22 5DH *Tel: 01962 849100* *Fax : 01962 849079* *provides consumer information and links to health sites*	www.hfht.org
Medical Research Council MRC Head Office, 20 Park Crescent, London W1N 4AL *Tel: 020 7636 5422* *Fax: 020 7436 6179*	www.mrc.ac.uk
National Electronic Library for Health	www.nelh.nhs.uk
Organising Medical Networked Information (OMNI) OMNI / BIOME, Greenfield Medical Library, Queens Medical Centre, Nottingham NG7 2UH	www.omni.ac.uk
NHS Direct	www.nhsdirect.nhs.uk
UK Health Centre *guide to health/medical information on the internet*	www.healthcentre.org.uk/hc/clinic/websites/default.htm
UK reference site for the lay person	www.patient.co.uk

References

1 Wolfe F, Zwillich SH. The long-term outcomes of rheumatoid arthritis: a 23-year prospective, longitudinal study of total joint replacement and its predictors in 1,600 patients with rheumatoid arthritis. Arthritis Rheum 1998; 41: 1072-82.

2 Pincus T. Rheumatoid arthritis: a medical emergency? Scand J Rheumatol Suppl 1994; 100: 21-30.

3 Wolfe F. The natural history of rheumatoid arthritis. J Rheumatol Suppl 1996; 44: 13-22.

4 Young A, Dixey J, Cox N, Davies P, Devlin J, Emery P, et al. How does functional disability in early rheumatoid arthritis (RA) affect patients and their lives? Results of 5 years of follow-up in 732 patients from the Early RA Study (ERAS). Rheumatol 2000; 39: 603-11.

5 Jantti J, Aho K, Kaarela K, Kautiainen H. Work disability in an inception cohort of patients with seropositive rheumatoid arthritis: a 20 year study. Rheumatology 1999; 38: 1138-41.

6 Cooper NJ. Economic burden of rheumatoid arthritis: a systematic review. Rheumatology 2000; 39: 28-33.

7 Emery P. The Roche Rheumatology Prize Lecture. The optimal management of early rheumatoid disease: the key to preventing disability. Br J Rheumatol 1994; 33: 765-8.

8 Emery P. Therapeutic approaches for early rheumatoid arthritis. How early? How aggressive? Br J Rheumatol 1995; 34 (suppl 2): 87-90.

9 Machold KP, Eberl G, Leeb BF, Nell V, Windisch B, Smolen JS. Early arthritis therapy: rationale and current approach. J Rheumatol Suppl 1998; 53: 13-9.

10 Brook A, Corbett M. Radiographic changes in early rheumatoid disease. Ann Rheum Dis 1977; 36: 71-73.

11 Fuchs HA, Kaye JJ, Callahan LF, Nance EP, Pincus T. Evidence of significant radiographic damage in rheumatoid arthritis within the first 2 years of disease. J Rheumatol 1989; 16: 585-591.

12 Kaarela K, Kautiainen H. Continuous progression of radiological destruction in seropositive rheumatoid arthritis. J Rheumatol 1997; 24: 1285-7.

13 Graudal NA, Jurik AG, de Carvalho A, Graudal HK . Radiographic progression in rheumatoid arthritis: a long-term prospective study of 109 patients. Arthritis Rheum 1998; 41: 1470-1480.

14 Drossaers-Bakker KW, de Buck M, van Zeben D, Zwinderman AH, Breedveld FC, Hazes JM. Long-term course and outcome of functional capacity in rheumatoid arthritis: the effect of disease activity and radiologic damage over time. Arthritis Rheum 1999; 42: 1854-60.

15 Symmons DP, Jones MA, Scott DL, Prior P. Longterm mortality outcome in patients with rheumatoid arthritis: early presenters continue to do well. J Rheumatol 1998; 25: 1072-7.

16 Arnett FC, Edworthy SM, Bloch DA, McShane DJ, Fries JF, Cooper NS, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum 1988; 31: 315-324.

17 Kirwan JR, Reeback JS. Stanford Health Assessment Questionnaire modified to assess disability in British patients with rheumatoid arthritis. Br J Rheumatol 1986; 25: 206-9.

18 Pincus T, Brooks RH, Callahan LF. Prediction of long-term mortality in patients with rheumatoid arthritis according to simple questionnaire and joint count measures. Ann Intern Med 1994; 120: 26-34.

19 Wolfe F, Ross K, Hawley DJ, Roberts FK, Cathey MA. The prognosis of rheumatoid arthritis and undifferentiated polyarthritis syndrome in the clinic: a study of 1141 patients. J Rheuamtol 1993; 20: 2005-9.

20 Mitchell DM, Spitz PW, Young DY, Bloch DA, McShane DJ, Fries J. Survival, prognosis and causes of death in Rheumatoid Arthritis. Arthritis Rheum 1986; 29: 706-14.

21 Devlin J, Gough A, Huissoon A, Perkins P, Holder R, Reece R et al. The acute phase and function in early rheumatoid arthritis. C-reactive protein levels correlate with functional outcome. J Rheumatol 1997; 24: 9-13.

22 van der Heijde DM, van Riel PL, van Leeuwen MA, van 't Hof MA, van Rijswijk MH, van de Putte LB. Prognostic factors for radiographic damage and physical disability in early rheumatoid arthritis. A prospective follow-up study of 147 patients. Br J Rheumatol 1992; 31: 519-25.

23 van Leeuwen MA, van der Heijde DM, van Rijswijk MH, Houtman PM, van Riel PL, van de Putte LB, et al. Interrelationship of outcome measures and process variables in early rheumatoid arthritis. A comparison of radiologic damage, physical disability, joint counts, and acute phase reactants. J Rheumatol 1994; 21: 425-9.

24 van Schaardenburg D, Hazes JM, de Boer A, Zwinderman AH, Meijers KA, Breedveld FC. Outcome of rheumatoid arthritis in relation to age and rheumatoid factor at diagnosis. J Rheumatol 1993; 20: 45-52.

25 Paimela L, Palosuo T, Leirisalo-Repo M, Helve T, Aho K. Prognostic value of quantitative measurement of rheumatoid factor in early rheumatoid arthritis. Br J Rheumatol 1995; 34: 1146-50.

26 Wolfe F, Hawley DJ. Remission in rheumatoid arthritis. J Rheumatol 1985; 12: 245-52.

27 Corbett M, Dalton S, Young A, Silman A, Shipley M. Factors predicting death, survival and functional outcome in a prospective study of early rheumatoid disease over fifteen years. Br J Rheumatol 1993; 32: 717-23.

28 Eberhardt KB, Fex E. Functional impairment and disability in early rheumatoid arthritis—development over 5 years. J Rheumatol 1995; 22: 1037-42.

29 Leigh JP, Fries JF. Predictors of disability in a longitudinal sample of patients with rheumatoid arthritis. Ann Rheum Dis 1992; 51: 581-7.

30 Callahan LF, Pincus T. Formal education level as a significant marker of clinical status in rheumatoid arthritis. Arthritis Rheum 1988; 31: 1346-57.

31 Callahan LF, Cordray DS, Wells G, Pincus T. Formal education and five-year mortality in rheumatoid arthritis: mediation by helplessness scale scores. Arthritis Care Res 1996; 9: 463-72.

32 McEntegart A, Morrison E, Capell HA, Duncan MR, Porter D, Madhok R, et al. Effect of social deprivation on disease severity and outcome in patients with rheumatoid arthritis. Ann Rheum Dis 1997; 56: 410-3.

33 Maiden N, Capell HA, Madhok R, Hampson R, Thomson EA. Does social disadvantage contribute to the excess mortality in rheumatoid arthritis patients? Ann Rheum Dis 1999; 58: 525-9.

34 ERAS Study Group. Socioeconomic deprivation and rheumatoid disease: what lessons for the health service? Ann Rheum Dis 2000; 59: 794-9.

35 Scott DL, Symmons DP, Coulton BL, Popert AJ. Long-term outcome of treating rheumatoid arthritis: results after 20 years. Lancet 1987; 1: 1108-11.

36 Fex E, Larsson BM, Nived K, Eberhardt K. Effect of rheumatoid arthritis on work status and social and leisure time activities in patients followed 8 years from onset. J Rheumatol 1998; 25: 44-50.

37 Capell HA, Murphy EA, Hunter JA. Rheumatoid arthritis: workload and outcome over 10 years. Q J Med 1991; 79: 461-76.

38 Vliet Vlieland TP, Breedveld FC, Hazes JM. The two-year follow-up of a randomized comparison of in patient multidisciplinary team care and routine out patient care for active rheumatoid arthritis. Br J Rheumatol 1997; 36: 82-5.

39 Pullar T, Hunter JA, Capell HA. Gold and penicillamine therapy: is shared care with general practitioners effective and safe? Rheumatol Rehabil.1982; 21: 139-44.

40 Holman HR, Lorig KR. Patient education: essential to good health care for patients with chronic arthritis. Arthritis Rheum 1997; 40: 1371-3.

41 Barlow JH, Wright CC. Knowledge in patients with rheumatoid arthritis: a longer term follow-up of a randomized controlled study of patient education leaflets. Br J Rheumatol 1998; 37; 373-6.

42 Superio-Cabuslay E, Ward MM, Lorig KR. Patient education interventions in osteoarthritis and rheumatoid arthritis: a meta-analytic comparison with nonsteroidal anti-inflammatory drug treatment. Arthritis Care Res 1996; 9: 292-301.

43 Evers AW, Kraaimaat FW, Geenen R, Bijlsma JW. Psychosocial predictors of functional change in recently diagnosed rheumatoid arthritis patients. Behav Res Ther 1998: 36: 179-93.

44 Lorig KR, Mazonson PD, Holman HR. Evidence suggesting that health education for self-management in patients with chronic arthritis has sustained health benefits while reducing health care costs. Arthritis Rheum 1993; 36: 439-46.

45 Kruger JM, Helmick CG, Callahan LF, Haddix AC. Cost-effectiveness of the arthritis self-help course. Arch Intern Med 1998; 158: 1245-9.

46 Anderson RB, Needleman RD, Gatter RA, Andrews RP, Scarola JA. Patient outcome following inpatient vs. outpatient treatment of rheumatoid arthritis. J Rheumatol 1988; 15: 556-60.

47 Helewa A, Bombardier C, Goldsmith CH, Menchions B, Smythe HA. Cost-effectiveness of inpatient and intensive outpatient treatment of rheumatoid arthritis. A randomized, controlled trial. Arthritis Rheum 1989; 32: 1505-14.

48 Lambert CM, Hurst NP, Forbes JF, Lochhead A, Macleod M, Nuki G. Is day care equivalent to inpatient care for active rheumatoid arthritis? Randomised controlled clinical and economic evaluation. BMJ 1998; 316: 965-9.

49 Yelin E, Wanke LE. An assessment of the annual and long-term direct costs of rheumatoid arthritis: the impact of poor function and functional decline. Arthritis Rheum 1999; 42: 1209-18.

50 Kobelt G, Eberhardt K, Jonsson L, Jonsson B. Economic consequence of the progression of rheumatoid arthritis in Sweden. Arthritis Rheum 1999; 42: 347-56.

51 Huskisson EC. Simple analgesics for arthritis. BMJ 1974; 4: 196-200.

52 Hardin JG Jr, Kirk KA. Comparative effectiveness of five analgesics for the pain of rheumatoid synovitis. J Rheumatol 1979; 6: 405 -12.

53 Brooks PM, Dougan MA, Mugford S, Meffin E. Comparative effectiveness of 5 analgesics in patients with rheumatoid arthritis and osteoarthritis. J Rheumatol 1982; 9: 723-6.

54 Emery P, Gibson T. A double-blind study of the simple analgesic nefopam in rheumatoid arthritis. Br J Rheumatol 1986; 25: 72 -6.

55 Seideman P, Melander A. Equianalgesic effects of paracetamol and indomethacin in rheumatoid arthritis. Br J Rheumatol 1988; 27: 117-22.

56 Furst DE. Are there differences among nonsteroidal anti-inflammatory drugs? Comparing acetylated salicylates, nonacetylated salicylates, and nonacetylated nonsteroidal anti-inflammatory drugs. Arthritis Rheum 1994; 37: 1-9.

57 Brooks PM, Day RO. Nonsteroidal anti-inflammatory drugs—differences and similarities. N Engl J Med 1991; 324: 1716-25.

58 British Medical Association, Royal Pharmaceutical Society of Great Britain. British National Formulary. No 40 (September 2000). NSAID Interactions. Appendix I: Interactions. 588-624.London: BMA, RPS, 2000.

59 Wolfe MM, Lichtenstein DR, Singh G. Gastrointestinal toxicity of nonsteroidal anti-inflammatory drugs. NEJM 1999; 340: 1888-99.

60 Fries JF, Spitz PW, Williams CA, Bloch DA, Singh G, Hubert HB. A toxicity index for comparison of side effects among different drugs. Arthritis Rheum 1990; 33: 121-30.

61 Morris AJ, Madhok R, Sturrock RD, Capell HA, MacKenzie JF. Enteroscopic diagnosis of small bowel ulceration in patients receiving non-steroidal anti-inflammatory drugs. Lancet 1991; 337: 520.

62 Scottish Intercollegiate Guidelines Network. Helicobacter pylori: eradication in dyspeptic disease. Edinburgh:SIGN 1996 (SIGN Publication No. 8).

63 Langman MJ, Weil J, Wainwright P, Lawson DH, Rawlins MD, Logan RF et al. Risks of bleeding peptic ulcer associated with individual non-steroidal anti-inflammatory drugs. Lancet 1994; 343: 1075-8.

64 Garcia Rodriquez LA, Jick, H. Risk of upper gastrointestinal bleeding and perforation associated with individual non-steroidal anti-inflammatory drugs. Lancet 1994; 343; 1048.

65 Hawkey CJ, Karrasch JA, Szczepanski L, Walker DG, Barkun A, Swannell AJ et al. Omeprazole compared with misoprostol for ulcers associated with nonsteroidal anti-inflammatory drugs. Omeprazole versus Misoprostol for NSAID-induced Ulcer Management (OMNIUM) Study Group. NEJM1998; 338: 727-34.

66 Silverstein FE, Graham DY, Senior JR, Davies HW, Struthers BJ, Bittman RM et al. Misoprostol reduces serious gastrointestinal complications in patients with rheumatoid arthritis receiving nonsteroidal anti-inflammatory drugs. A randomized, double-blind, placebo-controlled trial. Ann Intern Med. 1995; 123: 241-9.

67 Swan SK, Rudy DW, Lasseter KC, Ryan CF, Buechel KL, Lambrecht LJ, et al. Effect of cyclooxygenase-2 inhibition on renal function in elderly persons receiving a low salt diet. A randomized controlled trial. Ann Intern Med 2000; 133:1-9.

68 Simon LS, Weaver AL, Graham DY, Kivitz AJ, Lipsky PE, Hubbard RC et al. Anti-inflammatory and upper gastrointestinal effects of celecoxib in rheumatoid arthritis: a randomised controlled trial. JAMA 1999; 282: 1921-8.

69 Emery P, Zeidler H, Kvien TK, Guslandi M, Naudin R, Stead H et al. Celecoxib versus diclofenac in long-term management of rheumatoid arthritis: randomised double-blind comparison. Lancet 1999; 354: 2106-11.

70 Bensen WG, Zhao SZ, Burke TA, Zabinski RA, Makuch RW, Maurath CJ, et al. Upper gastrointestinal tolerability of celecoxib, a COX-2 specific inhibitor, compared to naproxen and placebo. J Rheumatol 2000; 27: 1876-83.

71 Silverstein FE, Faich G, Goldstein JL, Simon LS, Pincus T, Whelton A, et al. Gastrointestinal toxicity with celecoxib vs nonsteroidal anti-inflammatory drugs for osteoarthritis and rheumatoid arthritis. The CLASS Study: a randomized controlled trial. JAMA 2000; 284: 1247-55.

72 Bombardier C, Laine L, Reicin A, Shapiro D, Burgos-Vargas R, Davis B et al for the VIGOR Study Group. Comparison of upper gastrointestinal toxicity of Refecoxib and Naproxen in patients with rheumatoid arthritis. NEJM 2000; 343: 1520-8.

73 Committee on Safety in Medicines and The Medicines Control Agency. Current problems in pharmaco-vigilance. September 2000; 26: 13.

74 Schnitzer TJ, Truitt K, Fleischmann R, Dalgin P, Block J, Zeng Q, et al. The safety profile, tolerability, and effective dose range of rofecoxib in the treatment of rheumatoid arthritis. Phase II Rofecoxib Rheumatoid Arthritis Study Group. Clin Ther 1999; 21: 1688-702.

75 Felson DT, Anderson JJ, Meenan RF. The comparative efficacy and toxicity of second-line drugs in rheumatoid arthritis. Results of two metaanalyses. Arthritis Rheum 1990; 33: 1449-61.

76 Felson DT, Anderson JJ, Meenan RF. Use of short-term efficacy /toxicity tradeoffs to select second-line drugs in rheumatoid arthritis. A metaanalysis of published clinical trials. Arthritis Rheum 1992; 35: 1117-25.

77 Andrews FM, Golding DN, Freeman AM et al. Controlled trial of D (-) penicillamine in severe rheumatoid arthritis. Lancet 1973; 1: 275-80.

78 Clark P, Casas E, Tugwell P, Medina C, Gheno C, Tenorio G et al. Hydroxychloroquine compared with placebo in rheumatoid arthritis. A randomized controlled trial. Ann Intern Med 1993; 119: 1067-71.

79 Golding JR, Andrews FM, Camp V, Day AT, Freeman AM, Golding DN et al. A randomised trial of hydroxychloroquine in early rheumatoid arthritis: the HERA study. Am J Med 1995; 98: 156-68.

80 Jessop JD, O'Sullivan MM, Lewis PA, Williams LA, Camilleri JP, Plant MJ et al. A long-term five-year randomized controlled trial of hydroxychloroquine, sodium aurothiomalate, auranofin and penicillamine in the treatment of patients with rheumatoid arthritis. Br J Rheumatol 1998; 37: 992-1002.

81 Munro R, Hampson R, McEntegart A, Thomson EA, Madhok R, Capell H. Improved functional outcome in patients with early rheumatoid arthritis treated with intramuscular gold: results of a five year prospective study. Ann Rheum Dis 1998; 57: 88-93.

82 Dijkmans BA, van Rijthoven AW, Goei The HS, Boers M, Cats A. Cyclosporine in rheumatoid arthritis. Semin Arthritis Rheum 1992; 22: 30-6.

83 Fries JF, Williams CA, Morfeld D, Singh G, Sibley J. Reduction in long-term disability in patients with rheumatoid arthritis by disease modifying anti-rheumatic drug-based treatment strategies. Arthritis Rheum 1996; 39: 616-22.

84 Borg G, Allander E, Lund B, Ber E, Brodin U, Pettersson H et al. Auranofin improves outcome in early rheumatoid arthritis. Results from a 2-year, double blind, placebo controlled study. Journal of Rheumatology 1988; 15: 1747-54.

85 Smolen JS, Kalden JR, Scott DL, Rozman B, Kvien TK, Larsen A et al. Efficacy and safety of leflunomide compared with placebo and sulphasalazine in active rheumatoid arthritis: a double-blind, randomised, multicentre trial. European Leflunomide Study Group. Lancet 1999; 353: 259-66.

86 Egsmose C, Lund B, Borg G, Pettersson H, Berg E, Brodin U et al. Patients with rheumatoid arthritis benefit from early 2nd line therapy: 5 year followup of a prospective double blind placebo controlled study. J Rheumatol 1995; 22: 2208-13.

87 van der Heide A, Jacobs JW, Bijlsma JW, Heurkens AH, van Booma-Frankfort C, van der Veen MJ et al. The effectiveness of early treatment with "second line" antirheumatic drugs. A randomized, controlled trial. Ann Intern Med 1996; 124: 699-707.

88 Tsakonas E, Fitzgerald AA, Fitzcharles MA, Cividino A, Thorne JC, M'Seffar A et al. Consequences of delayed therapy with second-line agents in rheumatoid arthritis: a 3 year follow up on the hydroxychloroquine in early rheumatoid arthritis (HERA) study. J Rheumatol 2000; 27: 623-9.

89 van Jaarsveld CH, Jacobs JW, van der Veen MJ, Blaauw AA, Kruize AA, Hofman DM, et al. Aggressive treatment in early rheumatoid arthritis: a randomised controlled trial. On behalf of the Rheumatic Research Foundation Utrecht, The Netherlands. Ann Rheum Dis 2000; 59: 468-77.

90 Stenger AA, Van Leeuwen MA, Houtman PM, Bruyn GA, Speerstra F, Barendsen BC et al. Early effective suppression of inflammation in rheumatoid arthritis reduces radiographic progression. Br J Rheumatol 1998;37:1157-63.

91 Zeidler HK, Kvien TK, Hannonen P, Wollheim FA, Forre O, Geidel H et al. Progression of joint damage in early active severe rheumatoid arthritis during 18 months of treatment: comparison of low-dose cyclosporin and parenteral gold. Br J Rheumatol 1998; 37: 874-82.

92 McEntegart A, Porter D, Capell HA, Thomson EA. Sulfasalazine has a better efficacy/toxicity profile than auranofin – evidence from a 5 year prospective randomized trial. J Rheumatol 1996; 23: 1887-90.

93 van der Heijde DM, van Riel PL, Nuver-Zwart IH, Gribnau FW, van de Putte LB. Effects of hydroxychloroquine and sulphasalazine on progression of joint damage in rheumatoid arthritis. Lancet 1989; 1: 1036-8.

94 Menninger H, Herborn G, Sander O, Blechschmidt J, Rau R. A 36 month comparative trial of methotrexate and gold sodium thiomalate in the treatment of early active and erosive rheumatoid arthritis. Br J Rheumatol 1998; 37: 1060-8.

95 Rau R, Herborn G, Menninger M, Sangha O. Progression in early erosive rheumatoid arthritis: 12 month results from a randomised controlled trial comparing methotrexate and gold sodium thiomalate. Br J Rheumatol 1998; 37: 1220-6.

96 Strand V, Cohen S, Schiff M, Weaver A, Fleischmann R, Cannon Get al. Treatment of active rheumatoid arthritis with leflunomide compared with placebo and methotrexate. Leflunomide Rheumatoid Arthritis Investigators Group. Arch Intern Med 1999; 159: 2542-50.

97 ten Wolde S, Breedveld FC, Hermans J, Vandenbroucke JP, van de Laar MA, Markusse HM et al. Randomised placebo-controlled study of stopping second-line drugs in rheumatoid arthritis. Lancet 1996; 347: 347-52.

98 Gotzsche PC, Hansen M, Stoltenberg M, Svendsen A, Beier J, Faarvang KL et al. Randomized, placebo controlled trial of withdrawal of slow-acting antirheumatic drugs and of observer bias in rheumatoid arthritis. Scan J Rheumatol 1996; 25: 194-9.

99 Sokka T, Hannonen P. Utility of disease modifying antirheumatic drugs in "sawtooth" strategy. A prospective study of early rheumatoid arthritis patients up to 15 years. Ann Rheum Dis 1999; 58: 618-22.

100 Fries JF. ARAMIS and toxicity measurement. (Arthritis Rheumatism and Aging Medical Information System). J Rheumatol 1995; 22: 995-7.

101 Beauparlant P, Papp K, Haraoui B. The incidence of cancer associated with the treatment of rheumatoid arthritis. Semin Arthritis Rheum 1999; 29: 148-58.

102 Baecklund E, Ekbom A, Sparen P, Feltelius N, Klareskog L. Disease activity and risk of lymphoma in patients with rheumatoid arthritis: nested case-control study. BMJ 1998; 317: 180-1.

103 Asten P, Barrett J, Symmons D. Risk of developing certain malignancies is related to duration of immunosuppressive drug exposure in patients with rheumatic diseases. J Rheumatol 1999; 26: 1705-14.

104 Furst DE, Lindsley H, Baethge B, Botstein GR, Caldwell J, Dietz F et al. Dose-loading with hydroxychloroquine improves the rate of response in early, active rheumatoid arthritis: a randomized, double-blind six-week trial with eighteen-week extension. Arthritis Rheum 1999; 42: 357-65.

105 A randomized trial of hydroxychloroquine in early rheumatoid arthritis: the HERA Study. Am J Med 1995; 98: 156-68.

106 Capell HA. Clinical efficacy of sulphasalazine - a review. Br J Rheumatol 1995; 34: 35-9.

107 Weinblatt ME, Reda D, Henderson W, Giobbie-Hurder A, Williams D, Diani A et al. Sulfasalazine treatment for rheumatoid arthritis: a metaanalysis of 15 randomized trials. J Rheumatol 1999; 26: 2123-30.

108 Box SA, Pullar T. Sulphasalazine in the treatment of rheumatoid arthritis. Br J Rheumatol 1997; 36: 382-6.

109 Alarcon GS, Tracy IC, Strand GM, Singh K, Macaluso M. Survival and drug discontinuation analyses in a large cohort of methotrexate treated rheumatoid arthritis patients. Ann Rheum Dis 1995; 54: 708-12.

110 van Ede AE, Laan RF, Blom HJ, De Abreu RA, van de Putte LB. Methotrexate in rheumatoid arthritis: an update with focus on mechanisms involved in toxicity. Semin Arthritis Rheum 1998; 27: 277-92.

111 Furst DE. The rational use of methotrexate in rheumatoid arthritis and other rheumatic diseases. Br J Rheumatol 1997; 36: 1196-204.

112 Suarez-Almazor ME, Spooner C, Belseck E. Penicillamine for rheumatoid arthritis (Cochrane Review). In: The Cochrane Library Issue 2, 2000. Oxford: Update Software.

113 Suarez-Almazor ME, Spooner C, Belseck E. Azathioprine for rheumatoid arthritis. (Cochrane Review). In: The Cochrane Library Issue 2, 2000. Oxford: Update Software.

114 Emery P, Breedveld FC, Lemmel EM, Kaltwasser JP, Dawes PT, Gomor B, et al. A comparison of the efficacy and safety of leflunomide and methotrexate for the treatment of rheumatoid arthritis. Rheumatol 2000; 39: 655-65.

115 Chaudhuri K, Torley N, Madhok R. Disease-modifying anti-rheumatic drugs. Cyclosporin. Br J Rheumatol 1997; 36: 1016-21.

116 Ocular toxicity and hydroxychloroquine: guidelines for screening (replacing RCOphth Guidelines 1993). London: Royal College of Ophthalmologists; 1998.

117 British Society for Rheumatology. National guidelines for the monitoring of second line drugs. London: The Society; 2000.

118 Hydroxychloroquine datasheet. Electronic Medicines Compendium (ABPI). http://emc.vhn.net/public

119 Bluhm GB, Sharp JT, Tilley BC, Alarcon GS, Cooper SM, Pillemer SR et al. Radiographic results from the Minocycline in Rheumatoid Arthritis (MIRA) Trial. J Rheumatol 1997; 24: 1295-302.

120 Kloppenburg M, Breedveld FC, Terwiel JP, Mallee C, Dijkmans BA. Minocycline in active rheumatoid arthritis. A double-blind, placebo-controlled trial. Arthritis Rheum 1994; 37:629-36.

121 Tilley BC, Alarcon GS, Heyse SP, Trentham DE, Neuner R, Kaplan DA et al. Minocycline in rheumatoid arthritis. A 48-week, double-blind, placebo-controlled trial. MIRA Trial Group. Ann Intern Med 1995; 122:81-9.

122 O'Dell JR, Paulsen G, Haire CE, Blakely K, Palmer W, Wees S et al. Treatment of early seropositive rheumatoid arthritis with minocycline: four-year followup of a double-blind, placebo-controlled trial. Arthritis Rheum 1999;42: 1691-5.

123 Ortiz Z, Shea B, Suarez-Almazor ME, Moher D, Wells GA, Tugwell P. The efficacy of folic acid and folinic acid in reducing methotrexate gastrointestinal toxicity in rheumatoid arthritis. A metaanalysis of randomized controlled trials. J Rheumatol 1998; 25: 36-43.

124 Sokka T, Mottonen T, Hannonen P. Disease-modifying anti-rheumatic drug use according to the 'sawtooth' treatment strategy improves the functional outcome in rheumatoid arthritis: results of a long-term follow-up study with review of the literature. Rheumatology 2000; 39: 34-42.

125 Felson DT, Anderson JJ, Meenan RF. The efficacy and toxicity of combination therapy in rheumatoid arthritis. A meta-analysis. Arthritis Rheum 1994; 37: 1487-91.

126 Willkens RF, Sharp JT, Stablein D, Marks C, Wortmann R. Comparison of azathioprine, methotrexate, and the combination of the two in the treatment of rheumatoid arthritis. A forty-eight-week controlled clinical trial with radiologic outcome assessment. Arthritis Rheum 1995; 38: 1799-806.

127 Faarvang KL, Egsmose C, Kryger P, Podenphant J, Ingeman-Nielsen M, Hansen TM. Hydroxychloroquine and sulphasalazine alone and in combination in rheumatoid arthritis: a randomised double blind trial. Ann Rheum Dis 1993; 52: 711-5.

128 O'Dell JR, Haire CE, Erikson N, Drymalski W, Palmer W, Eckhoff PJ et al. Treatment of rheumatoid arthritis with methotrexate alone, sulfasalazine and hydroxychloroquine, or a combination of all three medications NEJM 1996; 334: 1287-91.

129 Haagsma CJ, van Riel PL, de Jong AJ, van de Putte LB. Combination of sulphasalazine and methotrexate versus the single components in early rheumatoid arthritis: a randomized, controlled, double-blind, 52 week clinical trial. Br J Rheumatol 1997; 36: 1082-8.

130 Dougados M, Combe B, Cantagrel A, Goupille P, Olive P, Schattenkirchner M et al. Combination therapy in early rheumatoid arthritis: a randomised, controlled, double blind 52 week clinical trial of sulphasalazine and methotrexate compared with the single components. Ann Rheum Dis 1999; 58: 22-5.

131 Mottonen T, Hannonen P, Leirisalo-Repo M, Nissila M, Kautiainen H, Korpela M. Comparison of combination therapy with single-drug therapy in early rheumatoid arthritis: a randomised trial. FIN-RACo trial group. Lancet 1999; 353: 1568-73.

132 Porter DR, Capell HA, Hunter J. Combination therapy in rheumatoid arthritis—no benefit of addition of hydroxychloroquine to patients with a suboptimal response to intramuscular gold therapy. J Rheumatol. 1993; 20: 645-9.

133 Tugwell P, Pincus T, Yocum D, Stein M, Gluck O, Kraag G et al. Combination therapy with cyclosporine and methotrexate in severe rheumatoid arthritis. The Methotrexate-Cyclosporine Combination Study Group. NEJM 1995; 333: 137-41.

134 Maini R, St Clair EW, Breedveld F, Furst D, Kalden J, Weisman M et al. Infliximab (chimeric anti-tumour necrosis factor alpha monoclonal antibody) versus placebo in rheumatoid arthritis patients receiving concomitant methotrexate: a randomised phase III trial. ATTRACT Study Group. Lancet 1999 Dec 4; 354: 1932-9.

135 Weinblatt ME, Kremer JM, Bankhurst AD, Bulpitt KJ, Fleischmann RM, Fox RI. A trial of etanercept, a recombinant tumor necrosis factor receptor: Fc fusion protein, in patients with rheumatoid arthritis receiving methotrexate. NEJM 1999; 340: 253-9.

136 Lipsky PE, van der Heijde DM, St Clair EW, Furst DE, Breedveld FC, Kalden JR, et al. Infliximab and methotrexate in the treatment of rheumatoid arthritis. NEJM 2000; 343: 1594-1602.

137 Boers M, Verhoeven AC, Markusse HM, van de Laar MA, Westhovens R, van Denderen JC et al. Randomised comparison of combined step-down prednisolone, methotrexate and sulphasalazine with sulphasalazine alone in early rheumatoid arthritis. Lancet 1997; 350: 309-18.

138 Proudman SM, Conaghan PG, Richardson C, Griffiths B, Green MJ, McGonagle RJ, et al. Treatment of poor prognosis early rheumatoid arthritis: a randomized study of treatment with methotrexate, cyclosporin a, and intraarticular corticosteroids compared with sulfasalazine alone. Arthritis Rheum 2000; 43: 1809-19.

139 Bathon JM, Martin RW, Fleischmann RM, Tesser JR, Schiff MH, Keystone EC. A comparison of etanercept and methotrexate in patients with early rheumatoid arthritis. NEJM 2000; 343: 1586-93.

140 Seror P, Pluvinage P, d'Andre FL, Benamou P, Attuil G. Frequency of sepsis after local corticosteroid injection (an inquiry on 1160000 injections in rheumatological private practice in France). Rheumatology 1999; 38: 1272-4.

141 Weitoft T, Uddenfeldt P. Importance of synovial fluid aspiration when injecting intra-articular corticosteroids. Ann Rheum Dis 2000; 59: 233-5.

142 Chakravarty K, Pharoah PD, Scott DG. A randomized controlled study of post-injection rest following intra-articular steroid therapy for knee synovitis. Br J Rheumatol 1994; 33: 464-8.

143 Laan RF, Jansen TL, van Riel PL. Glucocorticosteroids in the management of rheumatoid arthritis. Rheumatology 1999; 38: 6-12.

144 Kirwan JR. The effect of glucocorticoids on joint destruction in rheumatoid arthritis. The Arthritis and Rheumatism Council Low-Dose Glucocorticoid Study Group. NEJM 1995; 333: 142-6.

145 Million R, Kellgren JH, Poole P, Jayson MI. Long-term study of management of rheumatoid arthritis. Lancet 1984; 1: 812-6.

146 Hickling P, Jacoby RK, Kirwan JR. Joint destruction after glucocorticoids are withdrawn in early rheumatoid arthritis. Arthritis and Rheumatism Council Low Dose Glucocorticoid Study Group. Br J Rheumatol 1998; 37: 930-6.

147 Baltzan MA, Suissa S, Bauer DC, Cummings SR. Hip fractures attributable to corticosteroid use. Study of Osteoporotic Fractures Group. Lancet 1999 17; 353: 1327.

148 Committee on Safety in Medicines and the Medicines Control Agency. Current problems in pharmacovigilance. London: The Committee; 2000. v.26, p.13.

149 Wolfe F, Mitchell DM, Sibley JT, Fries JF, Bloch DA, Williams CA et al. The mortality of rheumatoid arthritis. Arthritis Rheumatol 1994; 37: 481-94.

150 McDougall R, Sibley J, Haga M, Russell A. Outcome in patients with rheumatoid arthritis receiving prednisone compared to matched controls. J Rheumatol 1994; 21: 1207-13.

151 Saag KG, Koehnke R, Caldwell JR, Brasington R, Burmeister LF, Zimmerman B et al. Low dose long-term corticosteroid therapy in rheumatoid arthritis: an analysis of serious adverse events. Am J Med 1994; 96: 115-23.

152 Saag KG. Low-dose corticosteroid therapy in rheumatoid arthritis: balancing the evidence. Am J Med 1997; Dec 29103(6A): 31S-39S.

153 Linde K, Clausius N, Ramirez G, Melchart D, Eitel F, Hedges LV, et al. Are the clinical effects of homeopathy placebo effects? A meta-analysis of placebo-controlled trials. Lancet 1997; 350: 834-43.

154 Andrade LE, Ferraz MB, Atra E, Castro A, Silva MS. A randomized controlled trial to evaluate the effectiveness of homeopathy in rheumatoid arthritis. Scand J Rheum 1991; 20: 204-8.

155 Gibson RG, Gibson SL, MacNeill AD, Buchanan WW. Homoeopathic therapy in rheumatoid arthritis: evaluation by double-blind clinical therapeutic trial. Br J Clin Pharmacol 1980; 9: 453-9.

156 Mills SY, Jacoby RK, Chacksfield M, Willoughby M. Effect of a proprietary herbal medicine on the relief of chronic arthritic pain: a double-blind study. Br J Rheumatol 1996; 35: 874-8.

157 Pattrick M, Heptinstall S, Doherty M. Feverfew in rheumatoid arthritis: a double blind, placebo controlled study. Ann Rheum Dis 1989; 48: 547-9.

158 Bhatt- Saunders D. Acupuncture for rheumatoid arthritis: an analysis of the literature. Semin Arthritis Rheum 1985; 4: 225-31.

159 David J, Townsend S, Sathanathan R, Kriss S, Dore CJ. The effect of acupuncture on patients with rheumatoid arthritis: a randomised, placebo-controlled cross-over study. Rheumatology 1999; 38: 864-9.

160 Huskisson EC, Scott J, Bryans R. Seatone is ineffective in RA. BMJ 1981; 282: 1358-9.

161 Larkin JG, Capell HA, Sturrock RD. Seatone in rheumatoid arthritis: a six-month placebo-controlled study. Ann Rheum Dis 1985; 44: 199-201.

162 Tarp U, Overvad K, Thorling EB, Graudal H, Hansen JC. Selenium treatment in rheumatoid arthritis. Scand J Rheumatol 1985; 14: 364-8.

163 Ernst E. Evidence-based complementary medicine: a contradiction in terms? Ann Rheum Dis 1999; 58: 69-70.

164 MacDonald AG, Murphy EA, Capell HA, Bankowska UZ, Ralston SH. Effects of hormone replacement therapy in rheumatoid arthritis: a double blind placebo-controlled study. Ann Rheum Dis 1994; 53: 54-7.

165 Hall GM, Daniels M, Huskisson EC, Spector TD. A randomised controlled trial of the effect of hormone replacement therapy on disease activity in postmenopausal rheumatoid arthritis. Ann Rheum Dis 1994; 53: 112-6.

166 Hall GM, Daniels M, Doyle DV, Spector TD. Effect of hormone replacement therapy on bone mass in rheumatoid arthritis patients treated with and without steroids. Arthritis Rheum 1994; 37: 1499-505.

167 Helewa A, Goldsmith CH, Lee P, Bombardier C, Hanes B, Smythe HA et al. Effects of occupational therapy home service on patients with rheumatoid arthritis. Lancet 1991; 337: 1453-6.

168 Hammond A, Lincoln N, Sutcliffe L. A crossover trial evaluating an educational-behavioural joint protection programme for people with rheumatoid arthritis. Patient Educ Couns 1999; 37: 19-32.

169 Bell MJ, Lineker SC, Wilkins AL, Goldsmith CH, Badley EM. A randomized controlled trial to evaluate the efficacy of community based physical therapy in the treatment of people with rheumatoid arthritis. J Rheumatol 1998; 25: 231-7.

170 Van den Ende CHM, Vliet Vlieland TPM, Munneke M, Hazes JMW. Dynamic exercise therapy for rheumatoid arthritis (Cochrane Review) In: The Cochrane Library Issue 2, 2000. Oxford: Update Software.

171 Bostrom C, Harms-Ringdahl K, Karreskog H, Nordemar R. Effects of static and dynamic shoulder rotator exercises in women with rheumatoid arthritis: a randomised comparison of impairment, disability, handicap, and health. Scand J Rheumatol 1998; 27: 281-90.

172 Ahern M, Nicholls E, Simionetta E, Clark M, Bond M. Clinical and physiological effects of hydrotherapy in rheumatic diseases. Clin Rehab 1995; 9: 204-12.

173 Hall J, Skevington SM, Maddison PJ, Chapman K. A randomized and controlled trial of hydrotherapy in rheumatoid arthritis. Arthritis Care Res 1996; 9: 206-15.

174 Verhagen AP, de Vet HC, de Bie RA, Kessels AG, Boers M, Knipschild PG. Taking baths: the efficacy of balneotherapy in patients with arthritis. A systematic review. J Rheumatol 1997; 24: 1964-71.

175 Ayling J, Marks, R. Efficacy of paraffin wax baths for rheumatoid arthritic hands. Physiotherapy 2000; 86: 190-201.

176 Goats GC, Hunter JA, Flett E, Stirling A. Low intensity laser and phototherapy for rheumatoid arthritis. Physiotherapy 1996; 82: 311-20.

177 Hall J, Clarke AK, Elvins DM, Ring EF. Low level laser therapy is ineffective in the management of rheumatoid arthritic finger joints. Br J Rheumatol 1994; 33: 142-7.

178 Heussler JK, Hinchey G, Margiotta E, Quinn R, Butler P, Martin J et al. A double blind randomised trial of low power laser treatment in rheumatoid arthritis. Ann Rheum Dis 1993; 52: 703-6.

179 Palmgren N, Jensen GF, Kaae K, Windelin M, Colohov HC. Low-power laser therapy in rheumatoid arthritis. Lasers in Medical Science 1989; 4: 193-6.

180 Konrad K. Randomised double blind placebo controlled study of ultrasonic treatment of the hands of rheumatoid arthritis patients. European Journal of Physical Medicine & Rehabilitation 1994; 4: 155-7.

181 Feinberg J. Effect of the arthritis health professional on compliance with use of resting hand splints by patients with rheumatoid arthritis. Arthritis Care Res 1992; 5: 17-23.

182 Callinan NJ, Mathiowetz V. Soft versus hard resting hand splints in rheumatoid arthritis: pain relief, preference, and compliance. Am J Occup Ther 1996; 50: 347-53.

183 Kjeken I, Moller G, Kvien TK. Use of commercially produced elastic wrist orthoses in chronic arthritis: a controlled study. Arthritis Care Res 1995; 8: 108-13.

184 Pagnotta A, Baron M, Korner-Bitensky N. The effect of a static wrist orthosis on hand function in individuals with rheumatoid arthritis. J Rheumatol 1998; 25: 879-85.

185 Stern EB, Ytterberg SR, Krug HE, Mahowald ML. Finger dexterity and hand function: effect of three commercial wrist extensor orthoses on patients with rheumatoid arthritis. Arthritis Care Res 1996; 9: 197-205.

186 Stern EB, Ytterberg SR, Krug HE, Mullin GT, Mahowald ML. Immediate and short-term effects of three commercial wrist extensor orthoses on grip strength and function in patients with rheumatoid arthritis. Arthrits Care Res 1996; 9: 42-50.

187 Locke M, Perry J, Campbell J Thomas L. Ankle and subtalar motion during gait in arthritic patients. Phys Ther 1984; 64: 504-9.

188 MacSween A, Brydson G, Hamilton J. The effect of custom moulded ethyl vinyl acetate foot orthoses on the gait of patients with rheumatoid arthritis. Foot 1999; 9:128-3.

189 Hodge MC, Bach TM, Carter MG. Novel Award First Prize Paper. Orthotic management of plantar pressure and pain in rheumatoid arthritis. Clinical Biomechanics 1999; 14: 567-75.

190 Scottish Intercollegiate Guidelines Network. Obesity in Scotland: integrating prevention and weight management. Edinburgh: SIGN 1996 (SIGN Publication No. 8).

191 Munro R, Capell HC. Prevalence of low body mass in rheumatoid arthritis: association with the acute phase response. Ann Rheum Dis 1997; 56: 326-9.

192 Helliwell M, Coombes EJ, Moody BJ, Batstone GF, Robertson JC. Nutritional status in patients with Rheumatoid Arthritis. Ann Rheum Dis 1984; 43: 386-90.

193 Haugen M, Fraser D, Forre O. Diet therapy for the patient with rheumatoid arthritis? Rheumatology 1999; 38: 1039-44.

194 Kjeldsen-Kragh J, Haugen M, Borchgrevink CF, Laerum E, Eek M, Mowinkel P et al. Controlled trial of fasting and one-year vegetarian diet in rheumatoid arthritis. Lancet 1991; 338: 899-902.

195 Fortin P, Lew RA, Liang MH, Wright EA, Beckett LA, Chalmers TC et al. Validation of a meta-analysis: The effects of fish oil in Rheumatoid Arthritis. J Clin Epidemiol 1995; 48: 1379-90.

196 Brezeski M. Evening primrose oil in patients with rheumatoid arthritis and side-effects of non-steroidal anti-inflammatory drugs. Br J Rheum 1991; 30: 370-2.

197 Leventhal LJ, Boyce EG, Zurier RB. Treatment of rheumatoid arthritis with blackcurrant seed oil. Br J Rheum 1994; 33: 847-52.

198 Felson DT, Anderson JJ, Boers M, Bombardier C, Furst D, Goldsmith C, et al. Americal College of Rheumatology preliminary definitiions of improvement in rheumatoid arthritis. Arthritis Rheum 1995; 38: 727-35.

199 van Gestel AM, Prevoo ML, van't Hof MA, van Rijswijk MH, van de Putte LB, van Riel PL. Development and validation of the European League Against Rheumatism response criteria for rheumatoid arthritis. Arthritis Rheum 1996; 39: 34-40.

200 Ritchie DM, Boyle JA, McInnes JM, Jasani MK, Dalakos TG, Grieveson P, et al. Clinical studies with an articular index for the assessment of joint tenderness in patients with rheumatoid arthritis. Q J Med 1968; 37: 393-406.

201 Sharp JT. An overview of radiographic analysis of joint damage in rheumatoid arthritis and its use in meta analysis. J Rheumatol 2000; 27: 254-60.

202 Kirwan J. Using the Larsen index to assess radiographic progression in rheumatoid arthritis. J Rheumatol 2000; 27: 264-8.

Update to printed guideline

11 Oct 2004

Withdrawal of Rofecoxib

The NSAID Rofecoxib is mentioned in Section 4.2.4 and Annex 10 of this guideline. This drug has been voluntarily withdrawn from the market by the manufacturers due to concerns about a possible increased risk of heart attack or stroke. Patients currently being prescribed Rofecoxib should be transferred to a suitable alternative NSAID. Further information about the reasons for withdrawal of the drug can be found on the US Federal Drug Administration Web site at http://www.fda.gov/medwatch/SAFETY/2004/safety04.htm#vioxx

SIGN

Management of early rheumatoid arthritis

SIGN Publication Number 48

Quick Reference Guide

CLINICAL FEATURES OF EARLY RHEUMATOID ARTHRITIS (RA)

Symptoms

- *Joint pain/swelling*
- *Stiffness following inactivity*
- *Systemic 'flu-like' features*

Signs

- *Synovitis*
- *Joint swelling/tenderness*
- *Extra-articular features*

INFLAMMATORY POLYARTHRITIS

Differential diagnosis

- Viral arthritis
- Reactive arthritis
- Seronegative spondyloarthropathy
- Connective tissue disease
- Polymyalgia rheumatica
- Polyarticular gout
- Fibromyalgia
- Medical conditions presenting with arthropathy

Helpful investigations

- Erythrocyte sedimentation rate (ESR) /C-reactive protein (CRP)
- Full blood count
- Urea & electrolytes
- Liver function tests
- Uric acid/synovial fluid analysis
- Urinalysis
- Rheumatoid factor
- Anti-nuclear antibody
- Radiology

Adverse prognostic features in early RA

- Many active joints
- High ESR or CRP at outset
- Positive rheumatoid factor
- Early radiological erosions
- Poorer scores of function at outset
- Adverse socio-economic circumstances and lower educational level

EARLY INITIATION OF TREATMENT

B **RA should be treated as early as possible with disease modifying anti-rheumatic drugs (DMARDs) to control symptoms and delay disease progression.**

☑ All patients with persistent inflammatory joint disease (>6-8 weeks duration) already receiving simple analgesics and nonsteroidal anti-inflammatory drugs (NSAIDs) should be considered for referral for specialist rheumatology opinion and DMARD therapy, preferably within 12 weeks.

THE ROLE OF THE MULTIDISCIPLINARY TEAM

☑ All patients with early RA should have access to a range of health professionals, including general practitioner, rheumatologist, nurse specialist, physiotherapist, occupational therapist, dietitian, podiatrist, pharmacist and social worker.

C **Skilled occupational therapy advice should be available to those experiencing limitations in function.**

C **Resting and working splints can be used to provide pain relief.**

B **Patients should be encouraged to undertake simple dynamic exercises.**

☑ Podiatry referral should be offered to all patients.

KEY A B C D indicates grade of recommendation ☑ good practice point

PHARMACOLOGICAL MANAGEMENT OF EARLY RA

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)

B **The lowest NSAID dose compatible with symptom relief should be prescribed. NSAIDs should be reduced and if possible withdrawn when a good response to DMARDs is achieved.**

B **Introduce gastro-protection in RA patients >65 years and in those with a past history of peptic ulcer.**

☑
- Simple analgesics should be used in place of NSAIDs if possible and DMARDs should be introduced early to suppress disease activity.
- Only one NSAID should be prescribed at a time.
- Prescribers should be aware of the many potential interactions with NSAIDs and the side effect profiles of different drugs.
- Consider intra-articular corticosteroids, particularly when disease is localised.
- NSAIDs should be avoided in patients taking anticoagulants or corticosteroids.

DISEASE MODIFYING ANTI-RHEUMATIC DRUGS (DMARDs)

B **Early DMARD therapy in RA is important to maintain function and reduce later disability.**

B **DMARD therapy should be sustained in inflammatory disease in order to maintain disease suppression.**

☑ DMARD choice should take into account patient preference and existing co-morbidity.

B **Sulphasalazine, methotrexate, IM gold, and penicillamine are equally effective DMARDs.**

B **Sulphasalazine and methotrexate are the current DMARDs of choice due to their more favourable efficacy/toxicity profiles.**

B **At present the balance of evidence does not support the routine use of combination DMARD therapy in early RA.**

☑ Patients should be counselled about the benefits and risks of specific DMARDs, and should be provided with additional written information.

☑ Clear advice about monitoring of specific DMARDs should be available to the patient, GP and practice nurse.

CORTICOSTEROID THERAPY

B **Oral corticosteroids are not recommended for routine use, as there is no sustained clinical or functional benefit and there is high risk of toxicity with long term use.**

D **The lowest possible dose of corticosteroid should be used for the shortest possible time.**

D **Monitor patients closely for adverse corticosteroid effects. Be alert to the possibility of diabetes, cataract and infection. Inform patients not previously infected of the danger of chicken pox/shingles exposure.**

☑ Inform patients of the risks of corticosteroids prior to prescription and issue a steroid warning card.

Derived from the national clinical guideline recommended for use in Scotland by the
Scottish Intercollegiate Guidelines Network (SIGN)
Royal College of Physicians of Edinburgh, 9 Queen Street, Edinburgh EH2 1JQ

This guideline was issued in December 2000 and will be reviewed in 2002.
Available on the SIGN website: www.sign.ac.uk